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<110> ROZEN, Rima

<120> cDNA FOR HUMAN METHYLENETETRAHYDROFOLATE
REDUCTASE AND USES THEREOF

<130> 04844/005005

<150> US 09/592,595

<151> 2000-06-12

<150> US 09/258,928

<151> 1999-03-01

<150> US 08/738,000

<151> 1997-02-12

<150> PCT/CA95/00314

<151> 1995-05-25

<150> GB 9410620.0

<151> 1994-05-26

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Pro Cys Leu Glu Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp	
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agt tcg aga tgt tcc acc ccg ggc ctg gac cct gag cgg cat gag aga	144
Ser Ser Arg Cys Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg	
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ctc cgg gag aag atg agg ccg cga ttg gaa tct ggt gac aag tgg ttc	192
Leu Arg Glu Lys Met Arg Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe	
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Ile Ser Arg Phe Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp	
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gtg acc tgg cac cca gca ggt gac cct ggc tca gac aag gag acc tcc	336
Val Thr Trp His Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser	
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Ser Met Met Ile Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr	
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Ile Leu His Met Thr Cys Cys Arg Gln Arg Leu Glu Glu Ile Thr Gly	
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cat ctg cac aaa gct aag cag ctg ggc ctg aag aac atc atg gcg ctg	480
His Leu His Lys Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu	
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Arg Gly Asp Pro Ile Gly Asp Gln Trp Glu Glu Glu Glu Gly Gly Phe	
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Asn Tyr Ala Val Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp	
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Tyr Phe Asp Ile Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala	
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Gly Ser Phe Glu Ala Asp Leu Lys His Leu Lys Glu Lys Val Ser Ala	
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Phe Arg Phe Val Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro Ile	
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Val Pro Gly Ile Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu	
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Val Lys Leu Ser Lys Leu Glu Val Pro Gln Glu Ile Lys Asp Val Ile	
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Glu Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu	
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Gly	Leu	His	Phe	Tyr	Thr	Leu	Asn	Arg	Glu	Met	Ala	Thr	Thr	Glu	Val	
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Trp	Ala	Leu	Ser	Ala	His	Pro	Lys	Arg	Arg	Glu	Glu	Asp	Val	Arg	Pro	
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Trp	Asp	Glu	Phe	Pro	Asn	Gly	Arg	Trp	Gly	Asn	Ser	Ser	Ser	Pro	Ala	
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Phe	Gly	Glu	Leu	Lys	Asp	Tyr	Tyr	Leu	Phe	Tyr	Leu	Lys	Ser	Lys	Ser	
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Gln	Gly	Ile	Leu	Thr	Ile	Asn	Ser	Gln	Pro	Asn	Ile	Asn	Gly	Lys	Pro	
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Ser	Ser	Asp	Pro	Ile	Val	Gly	Trp	Gly	Pro	Ser	Gly	Gly	Tyr	Val	Phe	
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Gln	Lys	Ala	Tyr	Leu	Glu	Phe	Phe	Thr	Ser	Arg	Glu	Thr	Ala	Glu	Ala	
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Leu	Leu	Gln	Val	Leu	Lys	Lys	Tyr	Glu	Leu	Arg	Val	Asn	Tyr	His	Leu	
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aat gct gtc act tgg ggc atc ttc cct ggg cga gag atc atc cag ccc 1728
Asn Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro
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acc gta gtg gat ccc gtc agc ttc atg ttc tgg aag gac gag gcc ttt 1776
Thr Val Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe
580 585 590

gcc ctg tgg att gag cgg tgg gga aag ctg tat gag gag gag tcc ccg 1824
Ala Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Glu Ser Pro
595 600 605

tcc cgc acc atc atc cag tac atc cac gac aac tac ttc ctg gtc aac 1872
Ser Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn
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645 650 655

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Thr Glu Ala Pro
660

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Ser Met Met Ile Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr
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Ser	Arg	Thr	Ile	Ile	Gln	Tyr	Ile	His	Asp	Asn	Tyr	Phe	Leu	Val	Asn
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Glu	Asp	Thr	Leu	Glu	Leu	Leu	Asn	Arg	Pro	Thr	Gln	Asn	Ala	Arg	Glu
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Thr Trp His Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser	
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	Gly Asp Pro Ile Gly Asp Gln Trp Glu Glu Glu Glu Gly Gly Phe Asn			
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	Tyr Ala Val Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp Tyr			
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	Phe Asp Ile Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala Gly			
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	Arg Phe Val Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro Ile Val			
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	Pro Gly Ile Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu Val			
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	cca atc aaa gac aac gat gct gcc atc cgc aac tat ggc atc gag ctg			915
	Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu Leu			
	290	295	300	
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Ser	Val	Phe	Glu	Val	Phe	Val	Leu	Tyr	Leu	Ser	Gly	Glu	Pro	Asn	Arg		
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Asn	Gly	His	Lys	Val	Thr	Cys	Leu	Pro	Trp	Asn	Asp	Glu	Pro	Leu	Ala		
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Gly	Ile	Leu	Thr	Ile	Asn	Ser	Gln	Pro	Asn	Ile	Asn	Gly	Lys	Pro	Ser		
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Ser	Asp	Pro	Ile	Val	Gly	Trp	Gly	Pro	Ser	Gly	Gly	Tyr	Val	Phe	Gln		
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Lys	Ala	Tyr	Leu	Glu	Phe	Phe	Thr	Ser	Arg	Glu	Thr	Ala	Glu	Ala	Leu		
		510			515				520						525		
ctg	caa	gtg	ctg	aag	aag	tac	gag	ctc	cgg	gtt	aat	tac	cac	ctt	gtc	1635	
Leu	Gln	Val	Leu	Lys	Lys	Tyr	Glu	Leu	Arg	Val	Asn	Tyr	His	Leu	Val		
				530					535					540			
aat	gtg	aag	ggt	gaa	aac	atc	acc	aat	gcc	cct	gaa	ctg	cag	ccg	aat	1683	
Asn	Val	Lys	Gly	Glu	Asn	Ile	Thr	Asn	Ala	Pro	Glu	Leu	Gln	Pro	Asn		
			545					550					555				
gct	gtc	act	tgg	ggc	atc	ttc	cct	ggg	cga	gag	atc	atc	cag	ccc	acc	1731	
Ala	Val	Thr	Trp	Gly	Ile	Phe	Pro	Gly	Arg	Glu	Ile	Ile	Gln	Pro	Thr		
		560					565					570					
gta	gtg	gat	ccc	gtc	agc	ttc	atg	ttc	tgg	aag	gac	gag	gcc	ttt	gcc	1779	
Val	Val	Asp	Pro	Val	Ser	Phe	Met	Phe	Trp	Lys	Asp	Glu	Ala	Phe	Ala		
		575				580					585						
ctg	tgg	att	gag	cgg	tgg	gga	aag	ctg	tat	gag	gag	gag	tcc	ccg	tcc	1827	
Leu	Trp	Ile	Glu	Arg	Trp	Gly	Lys	Leu	Tyr	Glu	Glu	Glu	Ser	Pro	Ser		
		590			595					600					605		
cgc	acc	atc	atc	cag	tac	atc	cac	gac	aac	tac	ttc	ctg	gtc	aac	ctg	1875	
Arg	Thr	Ile	Ile	Gln	Tyr	Ile	His	Asp	Asn	Tyr	Phe	Leu	Val	Asn	Leu		
				610					615					620			

gtg gac aat gac ttc cca ctg gac aac tgc ctc tgg cag gtg gtg gaa 1923
Val Asp Asn Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val Glu
625 630 635

gac aca ttg gag ctt ctc aac agg ccc acc cag aat gcg aga gaa acg 1971
Asp Thr Leu Glu Leu Leu Asn Arg Pro Thr Gln Asn Ala Arg Glu Thr
640 645 650

gag gct cca tga cctgcgtcc tgacgccctg cgttggagcc actcctgtcc 2023
Glu Ala Pro *
655

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Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp Ser Ser Arg Cys
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Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg Leu Arg Glu Lys
35 40 45
Met Arg Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe Ser Leu Glu Phe
50 55 60
Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu Ile Ser Arg Phe
65 70 75 80
Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp Val Thr Trp His
85 90 95
Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser Met Met Ile
100 105 110
Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr Ile Leu His Met
115 120 125
Thr Cys Cys Arg Gln Arg Leu Glu Glu Ile Thr Gly His Leu His Lys
130 135 140
Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu Arg Gly Asp Pro
145 150 155 160
Ile Gly Asp Gln Trp Glu Glu Glu Glu Gly Gly Phe Asn Tyr Ala Val
165 170 175
Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp Tyr Phe Asp Ile
180 185 190
Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala Gly Ser Phe Glu
195 200 205
Ala Asp Leu Lys His Leu Lys Glu Lys Val Ser Ala Gly Ala Asp Phe
210 215 220
Ile Ile Thr Gln Leu Phe Phe Glu Ala Asp Thr Phe Phe Arg Phe Val
225 230 235 240
Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro Ile Val Pro Gly Ile
245 250 255
Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu Val Lys Leu Ser
260 265 270
Lys Leu Glu Val Pro Gln Glu Ile Lys Asp Val Ile Glu Pro Ile Lys
275 280 285

Asp	Asn	Asp	Ala	Ala	Ile	Arg	Asn	Tyr	Gly	Ile	Glu	Leu	Ala	Val	Ser
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Leu	Cys	Gln	Glu	Leu	Leu	Ala	Ser	Gly	Leu	Val	Pro	Gly	Leu	His	Phe
305					310					315					320
Tyr	Thr	Leu	Asn	Arg	Glu	Met	Ala	Thr	Thr	Glu	Val	Leu	Lys	Arg	Leu
			325						330					335	
Gly	Met	Trp	Thr	Glu	Asp	Pro	Arg	Arg	Pro	Leu	Pro	Trp	Ala	Leu	Ser
			340					345					350		
Ala	His	Pro	Lys	Arg	Arg	Glu	Glu	Asp	Val	Arg	Pro	Ile	Phe	Trp	Ala
		355					360					365			
Ser	Arg	Pro	Lys	Ser	Tyr	Ile	Tyr	Arg	Thr	Gln	Glu	Trp	Asp	Glu	Phe
	370					375					380				
Pro	Asn	Gly	Arg	Trp	Gly	Asn	Ser	Ser	Ser	Pro	Ala	Phe	Gly	Glu	Leu
385					390					395					400
Lys	Asp	Tyr	Tyr	Leu	Phe	Tyr	Leu	Lys	Ser	Lys	Ser	Pro	Lys	Glu	Glu
			405					410						415	
Leu	Leu	Lys	Met	Trp	Gly	Glu	Glu	Leu	Thr	Ser	Glu	Ala	Ser	Val	Phe
			420				425						430		
Glu	Val	Phe	Val	Leu	Tyr	Leu	Ser	Gly	Glu	Pro	Asn	Arg	Asn	Gly	His
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Lys	Val	Thr	Cys	Leu	Pro	Trp	Asn	Asp	Glu	Pro	Leu	Ala	Ala	Glu	Thr
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Ser	Leu	Leu	Lys	Glu	Glu	Leu	Leu	Arg	Val	Asn	Arg	Gln	Gly	Ile	Leu
465					470					475					480
Thr	Ile	Asn	Ser	Gln	Pro	Asn	Ile	Asn	Gly	Lys	Pro	Ser	Ser	Asp	Pro
			485						490					495	
Ile	Val	Gly	Trp	Gly	Pro	Ser	Gly	Gly	Tyr	Val	Phe	Gln	Lys	Ala	Tyr
		500					505					510			
Leu	Glu	Phe	Phe	Thr	Ser	Arg	Glu	Thr	Ala	Glu	Ala	Leu	Leu	Gln	Val
		515					520					525			
Leu	Lys	Lys	Tyr	Glu	Leu	Arg	Val	Asn	Tyr	His	Leu	Val	Asn	Val	Lys
	530					535					540				
Gly	Glu	Asn	Ile	Thr	Asn	Ala	Pro	Glu	Leu	Gln	Pro	Asn	Ala	Val	Thr
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Trp	Gly	Ile	Phe	Pro	Gly	Arg	Glu	Ile	Ile	Gln	Pro	Thr	Val	Val	Asp
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		580						585					590		
Glu	Arg	Trp	Gly	Lys	Leu	Tyr	Glu	Glu	Glu	Ser	Pro	Ser	Arg	Thr	Ile
		595					600					605			
Ile	Gln	Tyr	Ile	His	Asp	Asn	Tyr	Phe	Leu	Val	Asn	Leu	Val	Asp	Asn
	610					615					620				
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